Acid-Base Pathophysiology in the Neonate and Infant

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ABSTRACT

The acid-base status of the fetus during the first stage of labor is a mild acidosis with moderate hypercapnia and a "numerically" severe hypoxemia (in which physiological adjustments allow for normal development). During the process of normal delivery, a transient asphyxia develops resulting in a more acidic pH, severe hypercapnia, and a further decrease of the partial pressure of oxygen (Po2) at birth. Maternal and fetal acid-base status should be evaluated simultaneously for proper interpretation; these must be interpreted in conjunction with fetal heart rate, pattern decelerations, and variability. Maternal respiratory acidosis or alkalosis results in rapid similar changes in the fetus prior to renal compensation in the mother. Adjustment by the fetus to a maternal metabolic acidosis or alkalosis is more prolonged and may not be identical to that of the mother. Fetal distress (acidosis) may be masked or erroneously exaggerated by its reaction to the maternal acid-base conditions. The present technique of intermittent fetal scalp blood sampling may be replaced by continuous monitoring scalp electrodes. Skin-puncture specimens in the neonate are satisfactory for serum pH and partial pressure of carbon dioxide (Pco2) but should not be utilized for Po2 studies (correlation is poor except for the 30 to 60 mmHg range of arterial partial pressure of oxygen [PaO2]). For the severely ill neonate, repeated blood samples should be obtained via vascular catheters rather than skin puncture. Transcutaneous Po2 electrodes are available for continuous monitoring of the oxygen status of the sick neonate; it is very likely that similar satisfactory transcutaneous electrodes for Pco2 will soon be available.

Introduction

The plasma electrolytes generally have similar concentrations in the adult, child, and newborn. In the newborn, potassium values are higher (4.0 to 7.6 mEq per liter). In contrast to adult values, phosphate is moderately higher in the child (physio-
logical growth) and much more so in the newborn (twice as high), whereas sulfate is moderately increased in the newborn. Phosphate and sulfate elevations are accentuated for infants on breast milk and more so when on cow’s milk. The large load of phosphate and sulfate present in cow’s milk causes a decrease of bicarbonate and total carbon dioxide content, with a small decrease of pH. The major alteration in acid-base balance is seen in the “well” premature infant who, in addition to having phosphate and sulfate levels as in the term neonate, has a 3-fold increase of organic acids resulting in a marked decrease of bicarbonate and total carbon dioxide content, with an average pH of 7.31. The premature infant also has a lower value for proteinate. These alterations are the result of relative immaturity of the kidneys and liver.

In 1962 Saling reported the technique of obtaining fetal scalp capillary blood during labor to determine pH, Fco₂, and Po₂. An acidicotic capillary pH was shown to be correlated to fetal depression at birth (Apgar score). Scalp blood pH values, collected within 15 minutes prior to delivery, correlated very well with umbilical artery samples. Because of the “lability” of fetal scalp pH, more than one capillary sample is needed to be able to follow the trend of a change. However, in serially obtained scalp capillary samples, the pH varied by 0.02 to 0.06. The reproducibility of serial scalp pH values depends upon the clinical situation. It is affected by maternal factors such as posture, medications, anesthesia, analgesia, hyperventilation, and uterine contractions and fetal factors such as cord compression and placental dysfunction.

Fetal Acid-Base Status

The evaluation of fetal acid-base status is indicated in the presence of fetal distress (“acidosis”) or certain clinical situations. Fetal distress may be evident by abnormal fetal heart rate (severe bradycardia or tachycardia) or alterations of the heart rate patterns such as late or variable decelerations and diminished or absent variability of the heart rate. Bradycardia can be caused by hypoxia or by direct depression from paracervical block anesthesia; tachycardia can be caused by chronic hypoxemia or, more frequently, result from fever of the mother. With average (six or more per minute) fetal heart rate variability, the mean fetal pH was higher than with decreased (five or less per minute) or absent variability. The fetal pH was significantly lower with more severe late decelerations (usually regarded as a sign of uteroplacental deficiency). Fetal hypoxia is also evident by the presence of meconium-stained amniotic fluid in the presence of a vertex presentation; the rectal sphincter is very sensitive to oxygen deprivation, resulting in the passage of fetal stools.

The normal pH of horse amniotic fluid is 6.93; the value for meconium-stained fluid was 6.60 in one example of metabolic acidosis and 6.42 in one with respiratory acidosis. The clinical situations in which acid-base evaluation of the fetus is indicated are maternal acidosis, fetal acidosis, metabolic acidosis, and respiratory acidosis. Potential sources of error during fetal acid-base monitoring are contamination with amniotic fluid; extremely slow blood flow; air bubbles in capillary tube; clotting of blood owing to slow collection, delayed or inadequate mixing, or insufficient or degenerated heparin; delay of collection of blood globule; inadequate sample size; relation of sample to uterine
contractions (best is just prior to an expected contraction); severe fetal caput formation; and acid-base status of the mother.\textsuperscript{17} Fetal scalp sampling may be unsuccessful because of fetal inaccessibility (membranes must be ruptured and cervix dilated three cm), excessive fetal hair, severe fetal acidosis with vasoconstriction and decreased blood flow, sudden onset of severe fetal distress, undiagnosed fetal death, and inadequate sampling paraphernalia.\textsuperscript{17} There are a few contraindications to fetal acid-base studies. These are premature labor with intact membranes, active maternal vaginal infections (syphilis, gonorrhea, or type II herpes simplex), compound breech presentation with no access to the fetal buttocks, and vertex presentation with only the fontanel accessible.\textsuperscript{17} Recent research efforts are involved with miniaturized glass electrodes for continuous measurement of fetal scalp tissue pH.\textsuperscript{310,38} Such developments will undoubtedly lead to replacement of intermittent fetal scalp blood sampling.

Fetal Blood in Relation to Maternal Blood

With each fetal blood sample, a maternal blood sample should be taken. It has been suggested that venous antecubital blood be obtained for ease of accessibility\textsuperscript{17} and because there is no significant difference between maternal blood samples from the brachial artery and cubital vein during labor.\textsuperscript{1} It is extremely important, when evaluating acid-base data in a neonate, to remember that adult reference values are not appropriate (figure 1). The values for the neonate (especially the low Pco\textsubscript{2} and low total carbon dioxide content) are closer to those of the pregnant woman during the third trimester.\textsuperscript{42} A difference of 0.10 between maternal and fetal pH is considered normal whereas a fetal pH more than 0.20 lower than the maternal value is considered to be a sign of fetal acidosis by some\textsuperscript{28} but not by others.\textsuperscript{33}

The presence of respiratory acidosis or alkalosis in the mother will result in a rapid similar change of fetal pH while the renal compensation in the mother will usually require hours or days. The increased Pco\textsubscript{2} in respiratory acidosis results in increased nonionic diffusion of carbon dioxide to the fetus where the pH also falls (acidosis) because of the decreased ratio of bicarbonate to carbonic acid (Henderson-Hasselbalch equation). Therefore, with maternal respiratory acidosis it is expected to find some respiratory acidosis in the fetus. Similarly, the high pH owing to maternal hyperventilation (low Pco\textsubscript{2}) causes the gradient to favor the transfer of carbon dioxide out from the fetal compartment, resulting in an increased ratio and an increased fetal pH. Such an increase of fetal pH owing to maternal “respiratory” factors may mask the presence of fetal distress (“acidosis”).

Adjustment by the fetus to a maternal metabolic acidosis or alkalosis is more prolonged and may not necessarily be identical to that present in the mother, depending upon the rapidity and extent of compensation occurring in the mother. In a maternal metabolic acidosis (reduced bicarbonate concentration and reduced pH), compensation is achieved by “immediate” hyperventilation (reduced Pco\textsubscript{2}). The concentration gradient favors the transfer of bicarbonate and carbon dioxide from the fetal to the maternal circulation. However, more carbon dioxide is moved across the placenta (nonionic diffusion) resulting in a relative increased Henderson-Hasselbalch ratio (bicarbonate to carbonic acid) with “alkalosis” in the fetus in the presence of maternal acidosis. Such fetal alkalosis in response to the maternal metabolic acidosis may mask a true distress (acidosis) in the fetus. Similarly, with maternal metabolic alkalosis (elevated bicarbonate and elevated pH), compensation is accomplished by hyperventilation (elevation of Pco\textsubscript{2}). The concentration gradient for bicarbonate and
carbon dioxide is from mother to fetus but the carbon dioxide is more readily transferred (nonionic), resulting in a decreased bicarbonate to carbonic acid ratio with fetal "acidosis" in the presence of maternal alkalosis. This can result in an erroneously larger pH difference between the mother and a fetus in distress (acidosis).

The normal adult respiratory volume of 5 liters per minute is increased in pregnancy to 10 liters per minute owing to the influence of progesterone causing a
chronic hyperventilation with a low PaCO₂. During labor the ventilatory rate can increase to as much as 35 liters per minute, resulting in a further decrease of PaCO₂, increased PaO₂, and elevated pH. During the first stage of labor, the fetus has a blood pH of about 7.35 (7.25 to 7.45) which decreases to 7.30 (7.25 to 7.35) during the second stage and falls to 7.25 (7.11 to 7.36) at birth (Table I). The Swiss Group for Neonatology considers neonatal acidosis owing to asphyxia to be present if the pH values are below 7.15, 7.20, and 7.25 for heelstick specimens obtained at 15, 30, and 60 minutes, respectively, after delivery. The fetal PCO₂ value for the first stage of labor is about 46 (44 to 48) and increases to 51 (37 to 79) mmHg at birth. During the first stage of labor, the fetal PO₂ is about 22 (16 to 24) mmHg and falls during the delivery to 8 to 24 mmHg at birth. The very low fetal PO₂ values gave rise to the concept that the fetus had the “environment of Mount Everest in utero”—comparable to the decreased oxygen seen at high altitudes. However, this does not mean that the fetus exists in an hypoxic environment since the compensatory mechanisms—increased hematocrit, increased cardiac output, and oxyhemoglobin dissociation curve shift to the left—allow for normal growth, utilizing more oxygen than the adult.

There is a significant correlation between the acid-base status of the fetus and the clinical condition of the newborn infant. However, a discrepancy was reported to exist in 18 percent of the infants. A false abnormal ("acidosis" present but no clinical depression at birth) is usually the result of the mother receiving medications or owing to excessive muscular activity during a long labor. There are many causes, however, of false normals (fetus has a "normal" pH but is depressed at birth). These are liberal administration of analgesia or anesthesia to the mother, precipitous delivery, obstetrical manipulations (difficult forceps

<table>
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<th>Parameter</th>
<th>pH</th>
<th>Pco₂ mmHg</th>
<th>Paco₂ mmHg</th>
<th>P50 mmHg</th>
<th>O₂Sat Percent</th>
<th>HCO₃ mmol/1</th>
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<td>Amniotic fluid</td>
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<td>53</td>
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<tr>
<td>Fetus†</td>
<td>7.25 - 7.45</td>
<td>44 - 48</td>
<td>16 - 24</td>
<td>30 - 50</td>
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<tr>
<td>At birth‡</td>
<td>7.11 - 7.36</td>
<td>37 - 79</td>
<td>8 - 24</td>
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<td>5 - 10 minutes</td>
<td>7.09 - 7.30</td>
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<td>33 - 75</td>
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<td>20 minutes</td>
<td>7.18 - 7.33</td>
<td>31 - 58</td>
<td>31 - 85</td>
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<td>30 minutes</td>
<td>7.21 - 7.38</td>
<td>28 - 54</td>
<td>31 - 85</td>
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<td>60 minutes</td>
<td>7.26 - 7.39</td>
<td>28 - 45</td>
<td>38 - 83</td>
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<td>After ‡ hour§</td>
<td>7.26 - 7.49</td>
<td>27 - 45</td>
<td>55 - 80</td>
<td>18 - 24</td>
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<td>One day</td>
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<td>27 - 40</td>
<td>54 - 95</td>
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<td>One week</td>
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<td>30 - 42</td>
<td>57 - 94</td>
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<td>Pregnant (at term) arterial</td>
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<td>26 - 37</td>
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<td>75 - 100</td>
<td>95 - 97.5</td>
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<td>venous</td>
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<td>30 - 50</td>
<td>25 - 28%</td>
<td>58 - 85</td>
<td>24 - 28</td>
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</table>

*Data based on references
†Fetal scalp capillary; first stage of labor
‡Umbilical artery
§Usually described as "newborn"
¶Adjusted to 50 percent saturation
Anoxia

Anoxia in the fetus, newborn, or adult causes all available tissue glucose and glycogen to be converted to lactic acid; tissue necrosis and brain edema will not develop if the lactate level does not exceed 18 to 20 $\mu$mol per gram of tissue if circulation and oxygen supplies are restored.22 Food-deprived monkeys were given infusions of saline or glucose (serum concentration increased 150 to 450 mg per dl) prior to exposure to cardiac arrest lasting 14 minutes.22 After resuscitation, the saline-treated group showed no or only minor injury to the nuclear structures of the brainstem, whereas the glucose-treated group manifested progressive neurologic deterioration and all died many hours later in cardiogenic shock. These findings are in contrast to the usual concept that two to four minutes of cardiac arrest causes brain injury, affecting the structures of the hemispheres, particularly the cortex.22

Blood Gas Analyses

The wide range of values for blood gas analyses in the neonate is related to the variability in obtaining a proper blood specimen from a skin puncture, especially if the studies are repeated many times. In such individuals an umbilical or peripheral arterial catheter should be utilized. Continuously recording intravascular oxygen electrodes have been used.24,43 It has been known since 1851 that the skin is permeable to oxygen; in normal individuals the cutaneous $P_{O_2}$ is about three to five mmHg, representing the excess above the metabolic needs of the skin.13 When transcutaneous electrodes are used, the sensor temperature is usually at 44° with skin temperature at 43° and capillary temperature at 41°.12 The higher than normal capillary temperature increases the basal blood flow more than 10 times to exceed one ml per g per minute, increasing the oxygen supply about 10-fold if the oxygen saturation is above 50 percent, decreasing to a small extent the oxygen solubility in plasma, and causing a shift to the right of the oxyhemoglobin dissociation curve. The net result is that the extra oxygen diffuses to the surface of the skin.13 There may be an error by not correcting the transcutaneous $P_{O_2}$ ($P_{tcO_2}$) value for the increased blood temperature or by overcorrecting it to the electrode temperature.35 Such electrodes have also been used in high risk patients during labor.39

The amount of power required for the heater to reach 44° has been used as an indicator of the blood flow; if increased power is needed to achieve 44°, it indicates a decrease of the circulation. The heating power is not a good reflection of tissue perfusion since 40 percent of the heat is lost to the environment via the sensor cable and 20 percent via the sensor per se; of the remaining 40 percent, only about half is blood flow dependent (dissipated via tissue blood flow).9 Transcutaneous $P_{O_2}$ values compare favorably to arterial $P_{O_2}$ ($PaO_2$) values in pediatric practice if the blood flow is adequate, whereas in adults the $P_{tcO_2}$ values are 20 percent lower than the $PaO_2$ values.41 In critically ill adults, the $P_{tcO_2}$ value was 79 ± 12 percent of the $PaO_2$ value when the cardiac index was greater than 2.2 liters per minute per m² (average 4.1).36 Tremper and Shoemaker obtain baseline values for $P_{tcO_2}$ and $PaO_2$ and then follow the individual with continuous $P_{tcO_2}$ determinations. If the $P_{tcO_2}$ falls, the $PaO_2$ is determined; a corresponding fall of $PaO_2$ denotes respiratory impairment whereas no major fall in $PaO_2$ signifies circulatory impairment.36 In severe shock with a car-
diac index less than 1.5 liters per minute per m², the PtcO₂ will gradually fall to zero.

Reported causes of impaired circulation which affect PtcO₂ values are shock, local shunting, congenital defects with shunting, skin necrosis, hypothermia, sclerema, hypoplastic left heart syndrome, subcutaneous emphysema, and therapy with alpha-adrenergic blockers.6,13,26 If the blood pressure in an infant is more than 2.5 standard deviations lower than the value expected for the birth weight, the PtcO₂ will be lower than the PaO₂41; a similar finding can be seen if the oxygen saturation is very low.13 It has been suggested that any infant with a low PtcO₂ value be checked for the presence of shock since the treatment for shock differs from that of arterial hypoxemia.29

Heelstick capillary blood should not be used to determine oxygen tension in the newborn since the value changes throughout the collection process. Studies compared to simultaneous PtcO₂ values revealed a mean relative change of −21 percent (range −67 to +63 percent).11 If skin puncture blood specimens are used, the goal should be to keep the Po₂ values above 30 mmHg to avoid hypoxemia but no higher than 60 mmHg to avoid oxygen toxicity. The high arterial oxygen values present with oxygen therapy are not reflected in the much lower capillary values. Full-term infants attain adult levels of Po₂ within the first three days of life. Premature infants (1200 to 2500 g) may need days to weeks to reach a "normal" Po₂ value, and infants who weigh less than 1200 g at birth may have low Po₂ levels for several months, usually requiring supplemental oxygen therapy.34 Even though there is a decrease of hemoglobin concentration during the first few months of life, the amount of oxygen released by the hemoglobin is increased. In premature infants (1000 to 1500 g) one ml of oxygen is released per 100 ml of blood at age one to two days and this is increased to 2.1 ml per 100 ml at nine to ten weeks of age.8 This occurs even though the hemoglobin concentration is reduced by half because of the gradual decrease in the proportion of hemoglobin F to hemoglobin A—resulting in a change in the shape and a shift to the right of the oxyhemoglobin dissociation curve.

A satisfactory Po₂ level does not necessarily equal a normal PaO₂ level. An elevated PaO₂ causes vasoconstriction of the pulmonary vessels and vasodilation of the cerebral vessels, whereas a decreased PaO₂ causes cerebral vasoconstriction and an elevation of lactate concentration.44 Transcutaneous carbon dioxide (PtcCO₂) electrodes have utilized infrared probes and vacuum chambers with mass spectrometry or gas chromatography techniques. The most promising development is a modification of the Stow-Severinghaus Pco₂ electrode using a sensor at 44°. There is a better correlation between PtcCO₂ and PaCO₂ in contrast to that between similar oxygen electrodes. However, the PtcCO₂ value is consistently higher than the PaCO₂; this is probably due to the smaller arterio-venous difference for carbon dioxide and the higher permeability of the skin for carbon dioxide gas.9 The PaCO₂ may be estimated from PtcCO₂ by including a correction factor for the temperature and metabolic activity of the skin or for the electronic or calibration values.9 In neonates with normoxia (PaO₂ greater than 40 mmHg), the PtcCO₂ correlated well with the PaCO₂; when PaO₂ was less than 40 mmHg (hypoxia), there was poor correlation with the PtcCO₂ values about twice those of PaCO₂.2 When the pH was above 7.30, the values for PtcCO₂ and PaCO₂ were well correlated; with pH less than 7.30, the correlation was poor. Both hypoxia and acidosis can affect tissue metabolism and the peripheral circulation.2 In dynamically stable surgical patients (cardiac index greater than 1.5 liters per minute per m²), the PtcCO₂ exceeds the
PaCO₂ by 23 ± 11 mmHg whereas in severe shock (cardiac index less than 1.5) the excess of the PtcCO₂ value increased to 61 ± 25 mmHg.37

References

30. SALING, E.: A new method for examination of the child during labor. Introduction, technique